



1/23

ATGGCAAATA	AAGCAGTAAA	TGACTTTATA	CTAGCTATGA	40
ATTACGATAA	AAAGAAACTC	TTGACCCATC	AGGGAGAAAG	80
TATTGAAAAT	CGTTTCATCA	AAGAGGGTAA	TCAGCTACCC	120
GATGAGTTTG	TTGTTATCGA	AAGAAAGAAG	CGGAGCTTGT	160
CGACAAATAC	AAGTGATATT	TCTGTAACAG	CTACCAACGA	200
CAGTCGCCTC	TATCCTGGAG	CACTTCTCGT	AGTGGATGAG	240
ACCTTGTTAG	AGAATAATCC	CACTCTTCTT	GCGGTCGATC	280
GTGCTCCGAT	GACTTATAGT	ATTGATTTGC	CTGGTTTGGC	320
AAGTAGCGAT	AGCTTTCTCC	AAGTGGAAGA	TCCCAGCAAT	360
TCAAGTGTTT	GCGGAGCGGT	AAACGATTTG	TTGGCTAAGT	400
GGCATCAAGA	TTATGGTCAG	GTCAATAATG	TCCCAGCTAG	440
AATGCAGTAT	GAAAAAATCA	CGGCTCACAG	CATGGAACAA	480
CTCAAGGTCA	AGTTTGGTTC	TGACTTTGAA	AAGACAGGGA	520
ATTCTCTTGA	TATTGATTTT	AACTCTGTCC	ATTCAGGCCA	560
AAAGCAGATT	CAGATTGTTA	ATTTTAAGCA	GATTTATTAT	600
ACAGTCAGCG	TAGACGCTGT	TAAAAATCCA	GGAGATGTGT	640
TTCAAGATAC	TGTAACGGTA	GAGGATTTAA	AACAGAGAGG	680
AATTTCTGCA	GAGCGTCCTT	TGGTCTATAT	TTCGAGTGTT	720
GCTTATGGGC	GCCAAGTCTA	TCTCAAGTTG	GAAACCACGA	760
GTAAGAGTGA	TGAAGTAGAG	GCTGCTTTTG	AAGCTTTGAT	800
AAAAGGAGTC	AAGGTAGCTC	CTCAGACAGA	GTGGAAGCAG	840
ATTTTGGACA	ATACAGAAGT	GAAGGCGGTT	ATTTTAGGGG	880
GCGACCCAAG	TTCGGGTGCC	CGAGTTGTAA	CAGGCAAGGT	920
GGATATGGTA	GAGGACTTGA	TTCAAGAAGG	CAGTCGCTTT	960

FIG. 1A



2/23

ACAGCAGATC	ATCCAGGCTT	GCCGATTTC	TATACAACTT	1000
CTTTTTTACG	TGACAATGTA	GTTGCGACCT	TTCAAAATAG	1040
TACAGACTAT	GTTGAGACTA	AGGTTACAGC	TTACAGAAAC	1080
GGAGATTTAC	TGCTGGATCA	TAGTGGTGCC	TATGTTGCCC	1120
AATATTATAT	TACTTGGAAT	GAATTATCCT	ATGATCATCA	1160
AGGTAAGGAA	GTCTTGACTC	CTAAGGCTTG	GGACAGAAAT	1200
GGGCAGGATT	TAACGGCTCA	CTTTACCACT	AGTATTCCTT	1240
TAAAAGGGAA	TGTTGTAAT	CTCTCTGTCA	AAATTAGAGA	1280
GTGTACCGGG	CTTGCTTGGG	AATGGTGGCG	TACGGTTTAT	1320
GAAAAAACCG	ATTTGCCACT	AGTGCGTAAG	CGGACGATTT	1360
CTATTTGGGG	AACAACCTCTC	TATCCGCAGG	TAGAAGATAA	1400
GGTAGAAAAT	GAC			1413

FIG. 1B


3/23



ATGGCAAATA AAGCAGTAAA TGA	CTTTATA CTAGCTATGA	40
ATTACGATAN ₅₀ AAAN ₅₄ AAACTC	TTGACCCATC AGGGAGAAAG	80
TATTGAAAAT CGTTTCAN ₉₈ CA	AAGAGGGTAA TCAGCTACCC	120
GN ₁₂₂ TGAGTTTG TTGN ₁₃₄ TAN ₁₃₇ CGA	AAGAAAGAAG CGGAGCTTGT	160
CGACAAATAC AAGTGATATT N ₁₈₁ CTGTAN ₁₈₇ CAG	CTACCN ₁₉₆ ACGA	200
CAGTCGCCTC TATCCTGGAG CACTTCTCGT	AGTGGATGAG	240
ACCTTGTN ₂₄₈ AG AGAATAATCC CACTCTTCTT	GCGGTN ₂₇₆ GATC	280
GTGCTCCGAT GACTTATAGT AN ₃₀₂ TGN ₃₀₅ TTTGC	CTGGTTTGGC	320
AAGTAGCGAT AGCTTTCTCC AAGTGGAAGA	N ₃₅₁ CCCAGCAAT	360
TCAAGTGTTT GCGGAGCGGN ₃₈₀ AN ₃₈₂ ACGATTTG	TTGGCTAAGT	400
GGCATCAAGA TTATGGTCAG GTCAATAATG	TCCCAGCTAG	440
AAAN ₄₄₃ GCAGTAT GAAAAAATN ₄₅₉ A	CGGCTCACAG CATGGAACAA	480
CTCAAGGTCA AGTTTGGTTC TGA	CTTTGAA AAGN ₅₁₄ CAGGGA	520
ATTCTCTTGA TATTGATTTT AACTCTGTCC	ATTCAGGN ₅₅₈ GA	560
AAAGCN ₅₆₆ GATT CAGATTGTTA ATN ₅₈₃ TTAAGCA	GATTTATTAT	600
ACAGTCAGCG TAGACGCTGT TAAAAATCCA	GGAGATGTGT	640
TTCAAGATAC TGTAACGGTA GAGGATTTAA	AACAGAGAGG	680
AATTTCTGCA GAGCGTCCTT TGGTCTATAT	TTCGAGN ₇₁₇ GTT	720
GCTTATGGGC GCCAAGTCTA TCTCAAGTTG	GAAACCACGA	760
GTAN ₇₆₄ GAGTGN ₇₇₀ TGAAGTAGAG	GCTGCTTTTG AAGCTTTGAT	800
AAAAGGAGTC AAGGTAGCTC CTCAGACAGA	GTGGAAGCAG	840
ATTTTGGACA ATACAGAAGT GAAGGCGGTT	ATTTTAGGGG	880
GCGACCCAAG TTCGGGTGCC CGAGTTGTAA	CAGGCAAGGT	920
GGATATGGTA GAGGACTTGA TTCAAGAAGG	CAGTCGCTTT	960
ACAGCAGATC ATCCAGGCTT GCCGATTTC	TATACAACTT	1000

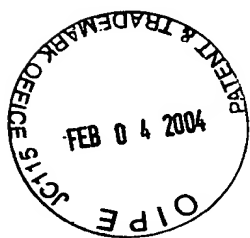
FIG. 2A

4/23



CTTTTTTACG TGACAATGTA GTTGCGACCT TTCAAAAN ₁₀₃₈ AG	1040
TACAGACTAT GTTGAGACTA AGGTTACAGC TTACAGAAAC	1080
GGAGATTTAC TGCTGGATCA TAGTGGTGCC TATGTTGCCC	1120
AATATTATAT TACTTGGN ₁₁₃₈ AT GAATTATCCT ATGATCATCA	1160
AGGTAAGGAA GTCTTGACTC CTAAGGCTTG GGACAGAAAT	1200
GGGCAGGATT TN ₁₂₁₂ ACGGCTCA CTTTACCACT AGTATTCCTT	1240
TAAAAGGGAA TGTTCGTAAT CTCTCTGTCA AAATTAGAGA	1280
GTGTACCGGG CTTGCN ₁₂₉₆ TGGG AATGGTGGCG TACGGTTTAT	1320
GAAAAAACCG ATTTGCCACT AGTGCGTAAG CGGACGATTT	1360
CTATTTGGGG AACAACTCTC TATCCN ₁₃₈₆ CAGG TAGAN ₁₃₉₅ GATAA	1400
GGTAGAAAAT GAC	1413

FIG. 2B



5/23

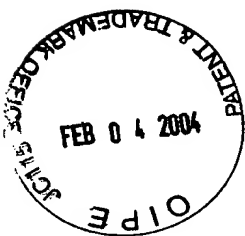
Met	Ala	Asn	Lys	Ala	Val	Asn	Asp	Phe	Ile	Leu	Ala	
1				5					10			
Met	Asn	Tyr	Asp	Lys	Lys	Lys	Leu	Leu	Thr	His	Gln	
		15					20					
Gly	Glu	Ser	Ile	Glu	Asn	Arg	Phe	Ile	Lys	Glu	Gly	
25				30						35		
Asn	Gln	Leu	Pro	Asp	Glu	Phe	Val	Val	Ile	Glu	Arg	
			40					45				
Lys	Lys	Arg	Ser	Leu	Ser	Thr	Asn	Thr	Ser	Asp	Ile	
	50					55					60	
Ser	Val	Thr	Ala	Thr	Asn	Asp	Ser	Arg	Leu	Tyr	Pro	
			65						70			
Gly	Ala	Leu	Leu	Val	Val	Asp	Glu	Thr	Leu	Leu	Glu	
		75					80					
Asn	Asn	Pro	Thr	Leu	Leu	Ala	Val	Asp	Arg	Ala	Pro	
85				90						95		
Met	Thr	Tyr	Ser	Ile	Asp	Leu	Pro	Gly	Leu	Ala	Ser	
			100					105				
Ser	Asp	Ser	Phe	Leu	Gln	Val	Glu	Asp	Pro	Ser	Asn	
	110					115					120	
Ser	Ser	Val	Arg	Gly	Ala	Val	Asn	Asp	Leu	Leu	Ala	
				125					130			
Lys	Trp	His	Gln	Asp	Tyr	Gly	Gln	Val	Asn	Asn	Val	
		135					140					
Pro	Ala	Arg	Met	Gln	Tyr	Glu	Lys	Ile	Thr	Ala	His	
145				150						155		
Ser	Met	Glu	Gln	Leu	Lys	Val	Lys	Phe	Gly	Ser	Asp	
			160					165				
Phe	Glu	Lys	Thr	Gly	Asn	Ser	Leu	Asp	Ile	Asp	Phe	
	170					175					180	
Asn	Ser	Val	His	Ser	Gly	Glu	Lys	Gln	Ile	Gln	Ile	
				185					190			
Val	Asn	Phe	Lys	Gln	Ile	Tyr	Tyr	Thr	Val	Ser	Val	
		195					200					
Asp	Ala	Val	Lys	Asn	Pro	Gly	Asp	Val	Phe	Gln	Asp	
205				210						215		
Thr	Val	Thr	Val	Glu	Asp	Leu	Lys	Gln	Arg	Gly	Ile	
			220					225				
Ser	Ala	Glu	Arg	Pro	Leu	Val	Tyr	Ile	Ser	Ser	Val	
	230					235					240	
Ala	Tyr	Gly	Arg	Gln	Val	Tyr	Leu	Lys	Leu	Glu	Thr	
				245					250			
Thr	Ser	Lys	Ser	Asp	Glu	Val	Glu	Ala	Ala	Phe	Glu	
		255					260					
Ala	Leu	Ile	Lys	Gly	Val	Lys	Val	Ala	Pro	Gln	Thr	
265				270						275		
Glu	Trp	Lys	Gln	Ile	Leu	Asp	Asn	Thr	Glu	Val	Lys	
			280					285				

FIG. 3A

6/23

Ala Val Ile Leu Gly Gly Asp Pro Ser Ser Gly Ala
290 295 300
Arg Val Val Thr Gly Lys Val Asp Met Val Glu Asp
305 310
Leu Ile Gln Glu Gly Ser Arg Phe Thr Ala Asp His
315 320
Pro Gly Leu Pro Ile Ser Tyr Thr Thr Ser Phe Leu
325 330 335
Arg Asp Asn Val Val Ala Thr Phe Gln Asn Ser Thr
340 345
Asp Tyr Val Glu Thr Lys Val Thr Ala Tyr Arg Asn
350 355 360
Gly Asp Leu Leu Leu Asp His Ser Gly Ala Tyr Val
365 370
Ala Gln Tyr Tyr Ile Thr Trp Asn Glu Leu Ser Tyr
375 380
Asp His Gln Gly Lys Glu Val Leu Thr Pro Lys Ala
385 390 395
Trp Asp Arg Asn Gly Gln Asp Leu Thr Ala His Phe
400 405
Thr Thr Ser Ile Pro Leu Lys Gly Asn Val Arg Asn
410 415 420
Leu Ser Val Lys Ile Arg Glu Cys Thr Gly Leu Ala
425 430
Trp Glu Trp Trp Arg Thr Val Tyr Glu Lys Thr Asp
435 440
Leu Pro Leu Val Arg Lys Arg Thr Ile Ser Ile Trp
445 450 455
Gly Thr Thr Leu Tyr Pro Gln Val Glu Asp Lys Val
460 465
Glu Asn Asp
470

FIG. 3B



7/23

Met	Ala	Asn	Lys	Ala	Val	Asn	Asp	Phe	Ile	Leu	Ala		
1				5					10				
Met	Asn	Tyr	Asp	Xaa	Xaa	Lys	Leu	Leu	Thr	His	Gln		
		15					20						
Gly	Glu	Ser	Ile	Glu	Asn	Arg	Phe	Xaa	Lys	Glu	Gly		
25				30						35			
Asn	Gln	Leu	Pro	Xaa	Glu	Phe	Val	Xaa	Xaa	Glu	Arg		
			40					45					
Lys	Lys	Arg	Ser	Leu	Ser	Thr	Asn	Thr	Ser	Asp	Ile		
	50					55				60			
Xaa	Val	Xaa	Ala	Thr	Xaa	Asp	Ser	Arg	Leu	Tyr	Pro		
			65						70				
Gly	Ala	Leu	Leu	Val	Val	Asp	Glu	Thr	Xaa	Leu	Glu		
		75				80							
Asn	Asn	Pro	Thr	Leu	Leu	Ala	Val	Asp	Arg	Ala	Pro		
85				90						95			
Met	Thr	Tyr	Ser	Xaa	Xaa	Leu	Pro	Gly	Leu	Ala	Ser		
			100					105					
Ser	Asp	Ser	Phe	Leu	Gln	Val	Glu	Asp	Pro	Ser	Asn		
	110				115					120			
Ser	Ser	Val	Arg	Gly	Ala	Xaa	Xaa	Asp	Leu	Leu	Ala		
				125					130				
Lys	Trp	His	Gln	Asp	Tyr	Gly	Gln	Val	Asn	Asn	Val		
		135				140							
Pro	Ala	Arg	Xaa	Gln	Tyr	Glu	Lys	Xaa	Thr	Ala	His		
145				150						155			
Ser	Met	Glu	Gln	Leu	Lys	Val	Lys	Phe	Gly	Ser	Asp		
			160					165					
Phe	Glu	Lys	Xaa	Gly	Asn	Ser	Leu	Asp	Ile	Asp	Phe		
	170				175					180			
Asn	Ser	Val	His	Ser	Gly	Glu	Lys	Xaa	Ile	Gln	Ile		
				185					190				
Val	Asn	Xaa	Lys	Gln	Ile	Tyr	Tyr	Thr	Val	Ser	Val		
		195				200							
Asp	Ala	Val	Lys	Asn	Pro	Gly	Asp	Val	Phe	Gln	Asp		
205				210						215			
Thr	Val	Thr	Val	Glu	Asp	Leu	Lys	Gln	Arg	Gly	Ile		
			220					225					
Ser	Ala	Glu	Arg	Pro	Leu	Val	Tyr	Ile	Ser	Xaa	Val		
	230				235					240			
Ala	Tyr	Xaa	Arg	Gln	Val	Tyr	Leu	Lys	Leu	Glu	Thr		
			245						250				
Thr	Ser	Xaa	Ser	Xaa	Glu	Val	Glu	Ala	Ala	Phe	Glu		
		255			260								
Ala	Leu	Ile	Lys	Gly	Val	Lys	Val	Ala	Pro	Gln	Thr		
265				270						275			
Glu	Trp	Lys	Gln	Ile	Leu	Asp	Asn	Thr	Xaa	Val	Lys		
			280					285					

FIG. 4A



8/23

Ala	Val	Ile	Leu	Gly	Gly	Asp	Pro	Ser	Ser	Gly	Ala
290						295					300
Arg	Val	Val	Thr	Gly	Lys	Val	Asp	Met	Val	Glu	Asp
				305					310		
Leu	Ile	Gln	Glu	Gly	Ser	Arg	Phe	Thr	Ala	Asp	His
		315					320				
Pro	Gly	Leu	Pro	Ile	Ser	Tyr	Thr	Thr	Ser	Phe	Leu
325					330					335	
Arg	Asp	Asn	Val	Val	Ala	Thr	Phe	Gln	Asn	Ser	Thr
			340					345			
Asp	Tyr	Val	Glu	Thr	Lys	Val	Thr	Ala	Tyr	Arg	Asn
	350					355					360
Gly	Asp	Leu	Leu	Leu	Asp	His	Ser	Gly	Ala	Tyr	Val
				365					370		
Ala	Gln	Tyr	Tyr	Ile	Thr	Trp	Xaa	Glu	Leu	Ser	Tyr
		375					380				
Asp	His	Gln	Gly	Lys	Glu	Val	Leu	Thr	Pro	Lys	Ala
385					390					395	
Trp	Asp	Arg	Asn	Gly	Gln	Asp	Leu	Thr	Ala	His	Phe
			400					405			
Thr	Thr	Ser	Ile	Pro	Leu	Lys	Gly	Asn	Val	Arg	Asn
	410					415					420
Leu	Ser	Val	Lys	Ile	Arg	Glu	Cys	Thr	Gly	Leu	Ala
				425					430		
Trp	Glu	Trp	Trp	Arg	Thr	Val	Tyr	Glu	Lys	Thr	Asp
		435					440				
Leu	Xaa	Leu	Val	Arg	Lys	Arg	Thr	Ile	Ser	Ile	Trp
445					450					455	
Gly	Thr	Thr	Leu	Tyr	Pro	Gln	Val	Glu	Asp	Lys	Val
			460					465			
Glu	Asn	Asp									
		470									

FIG. 4B

9 / 23

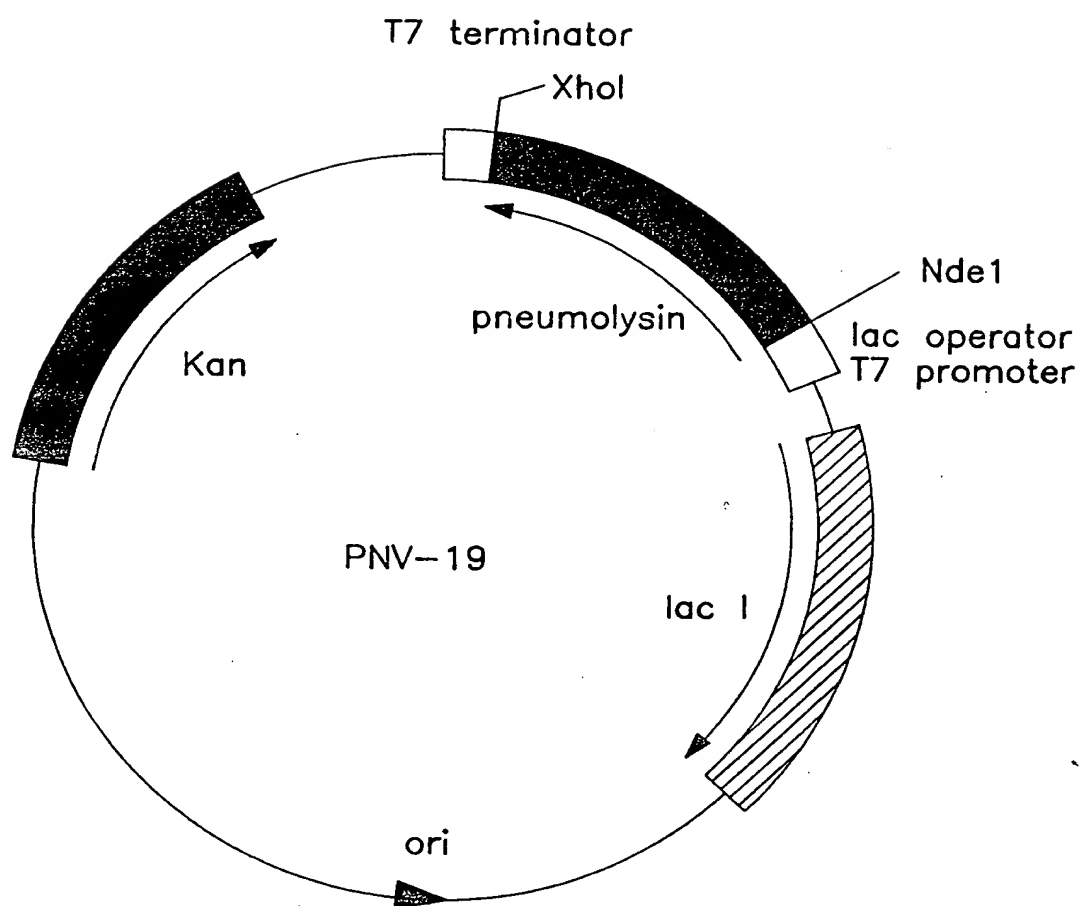


FIG. 5





11 / 23

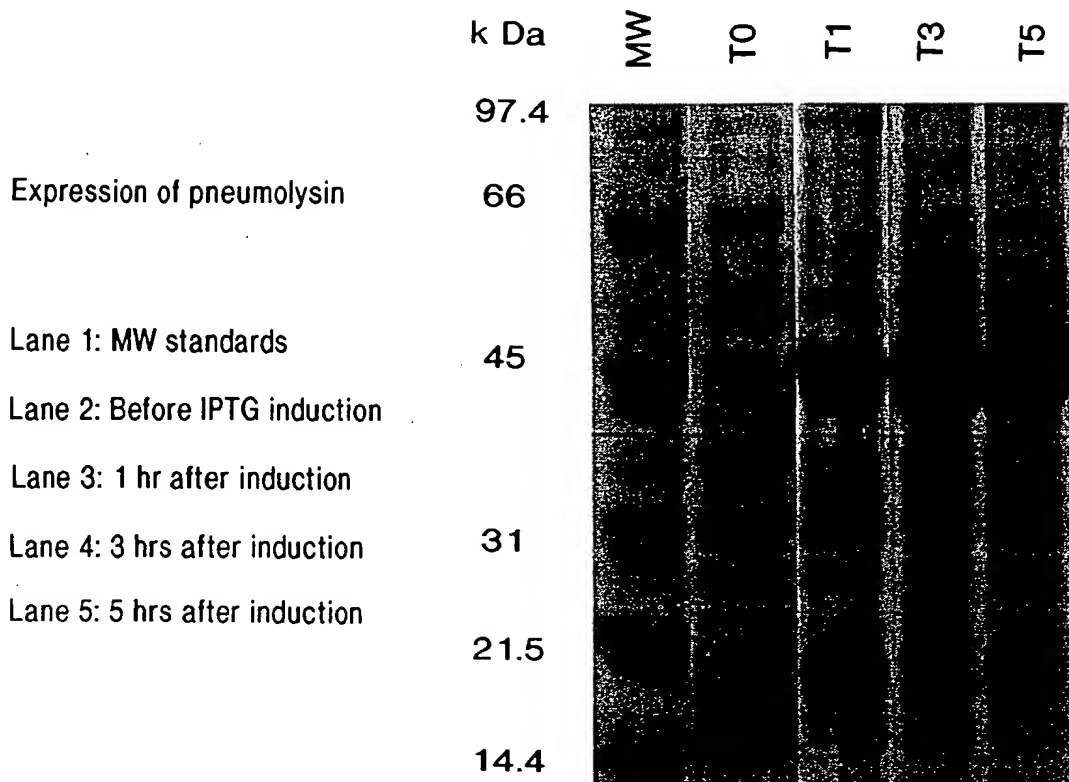


FIG. 7



12 / 23

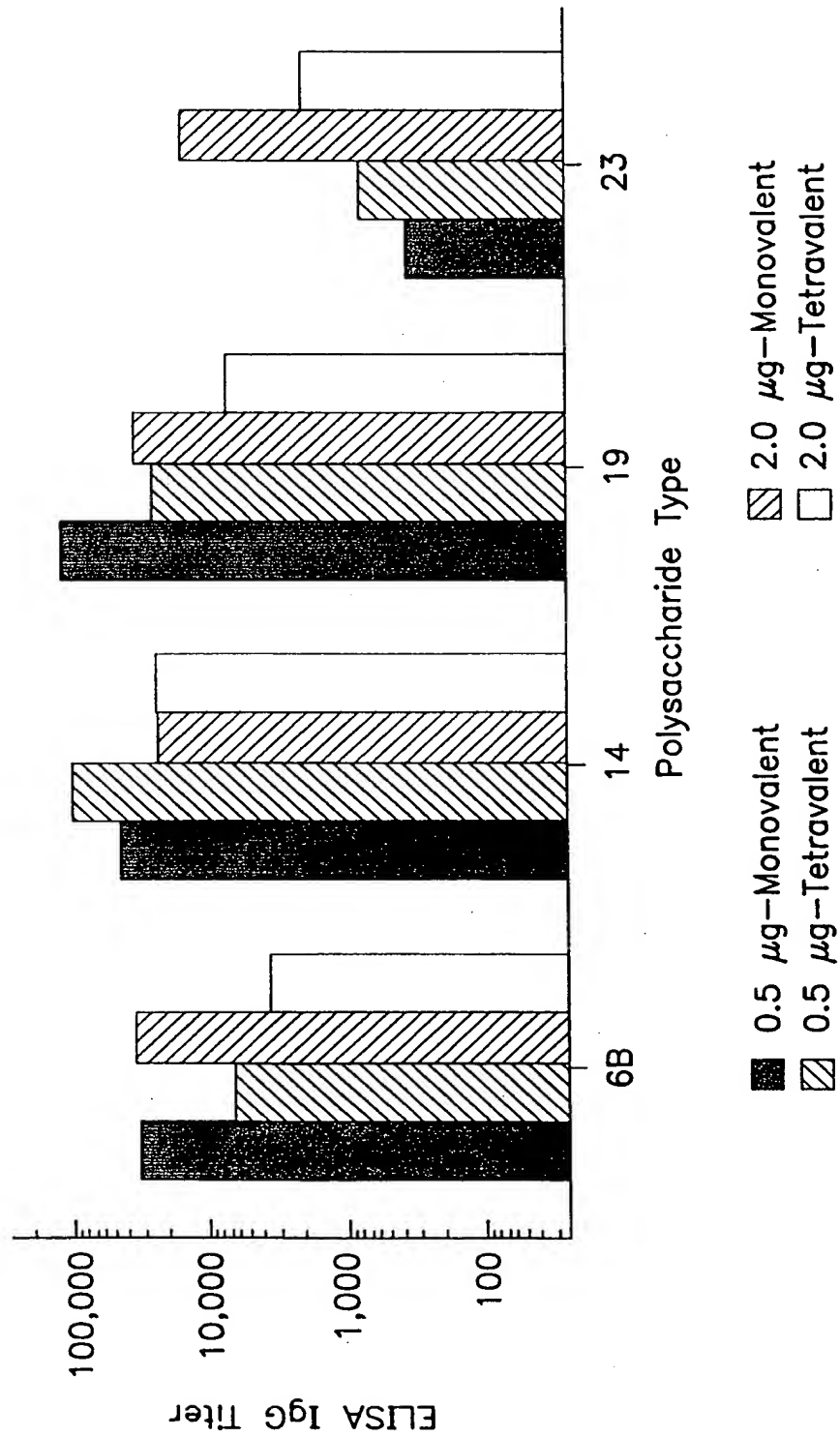
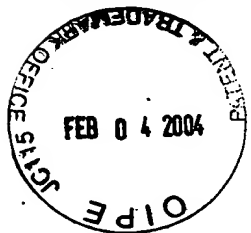


FIG. 8



13 / 23

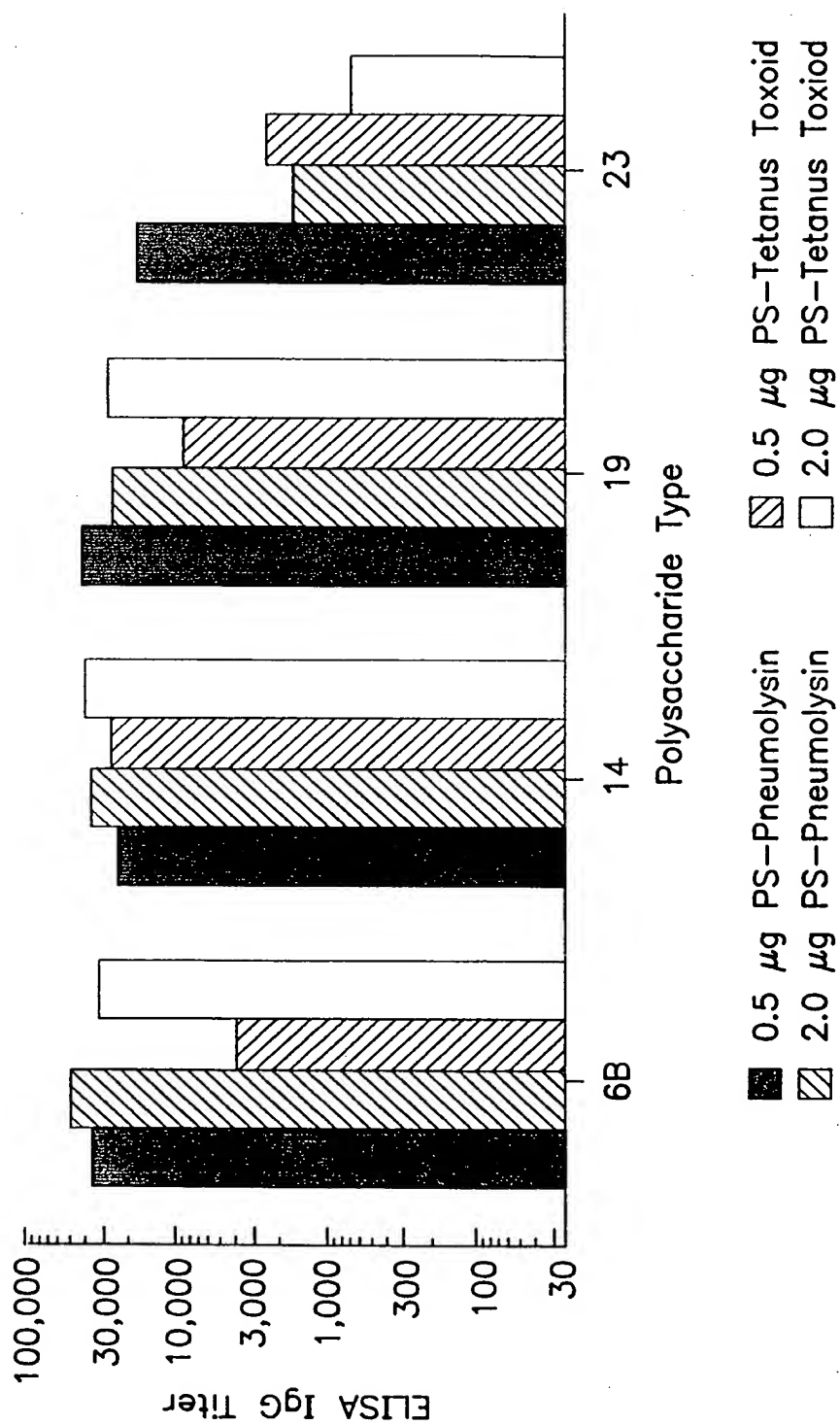


FIG. 9



14/23

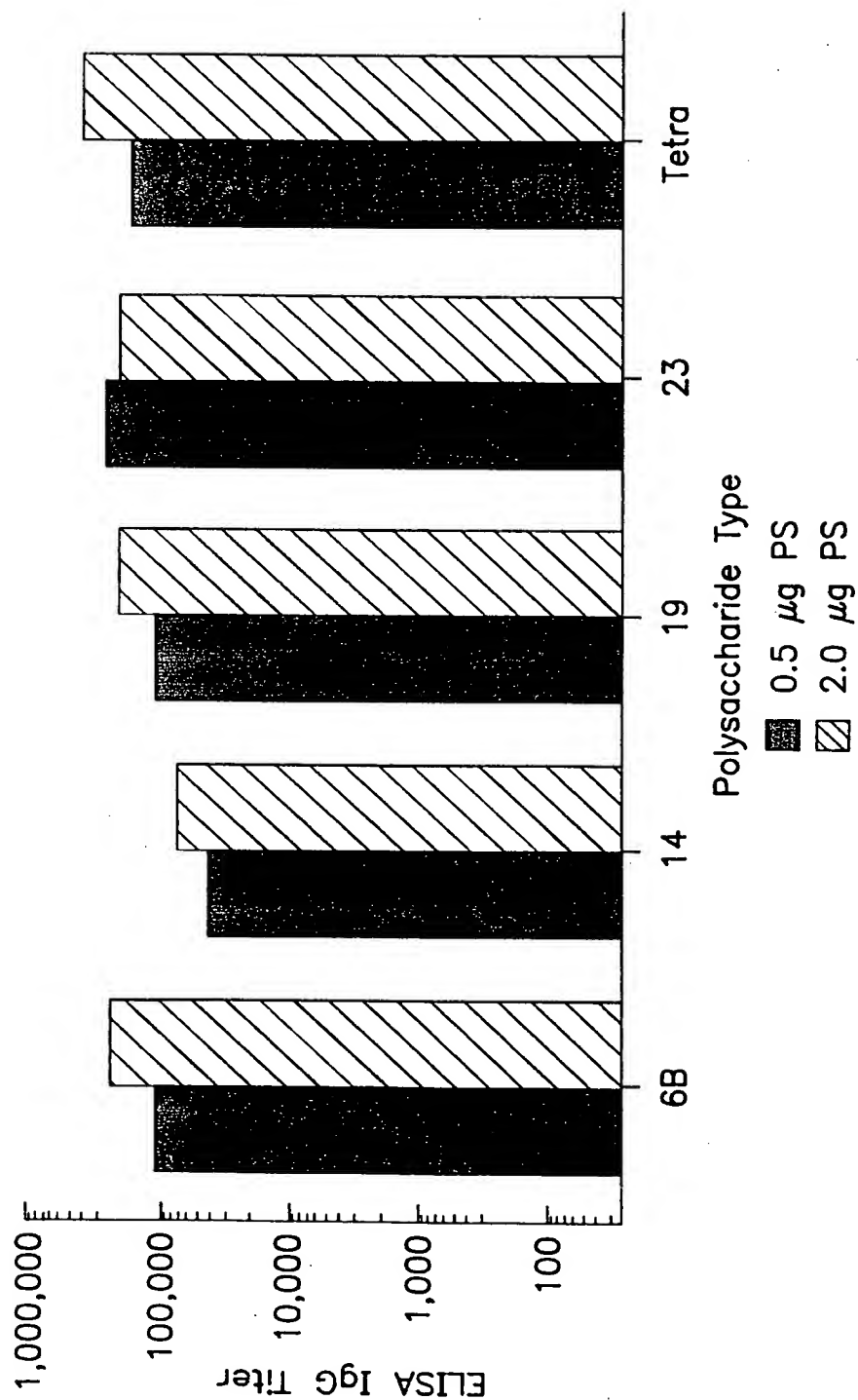


FIG. 10

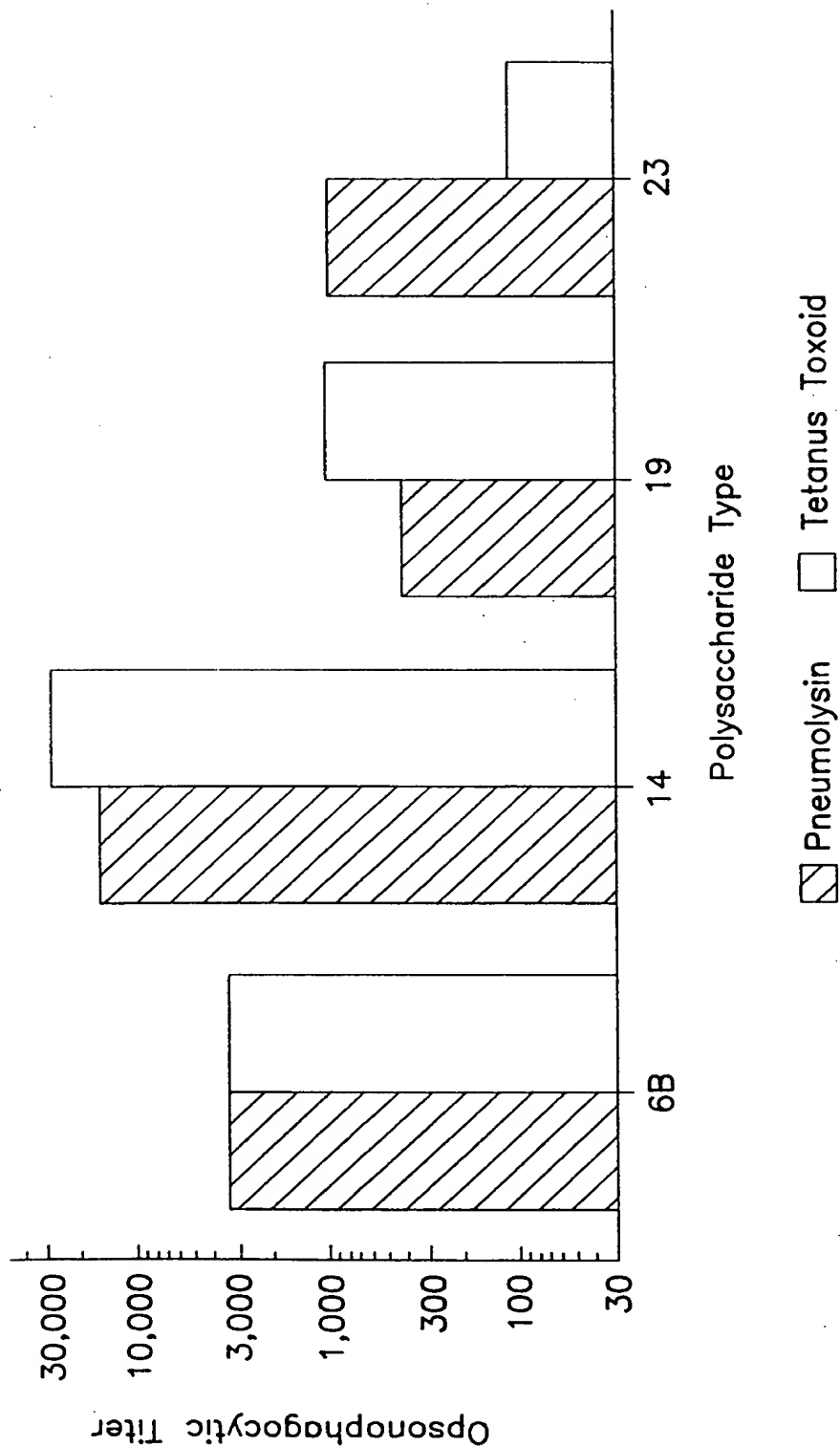
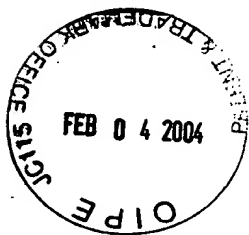


FIG. II

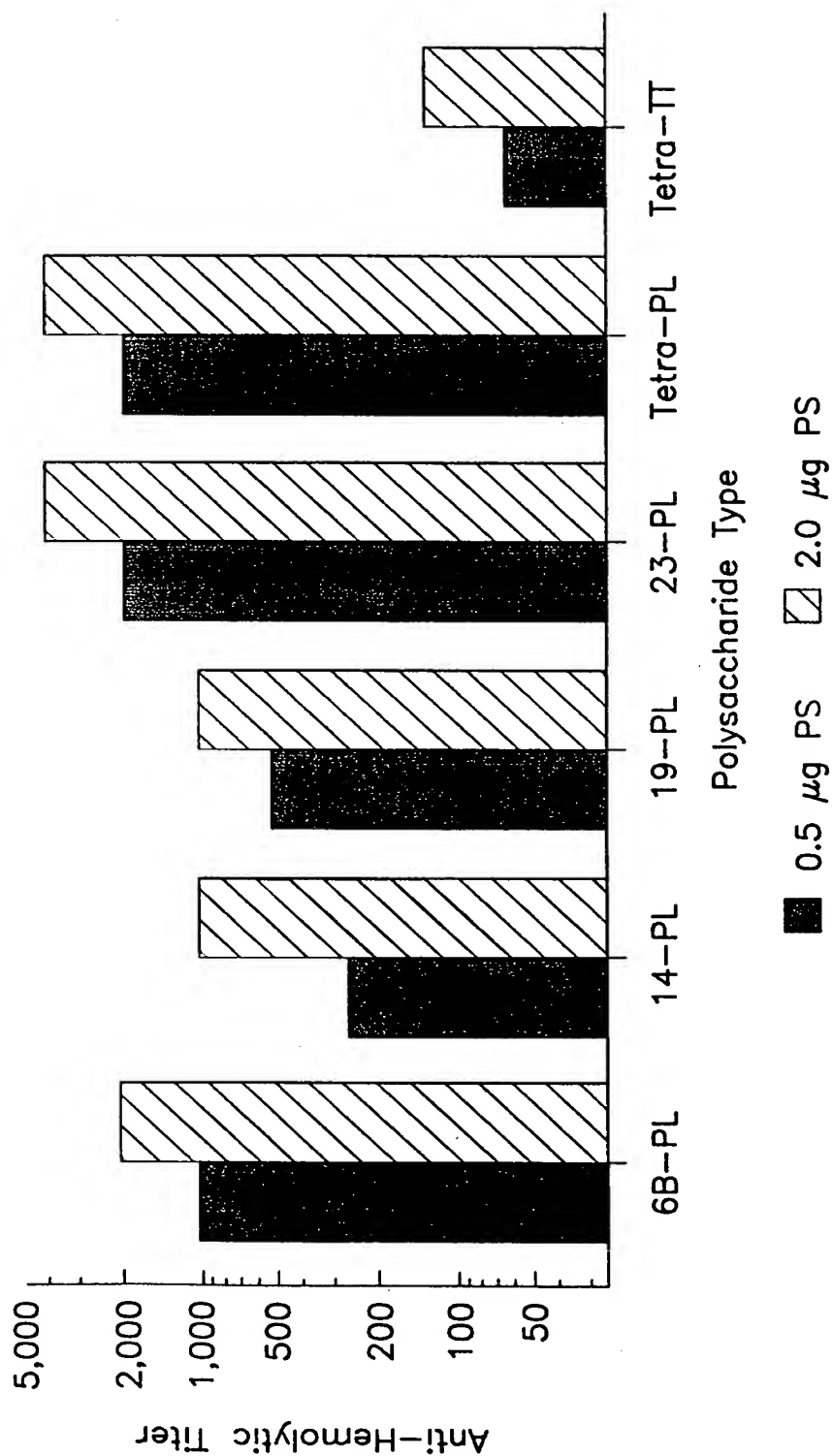
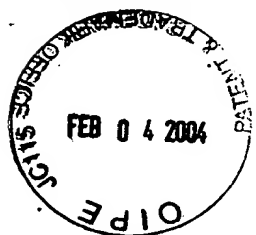


FIG. 12



17 / 23

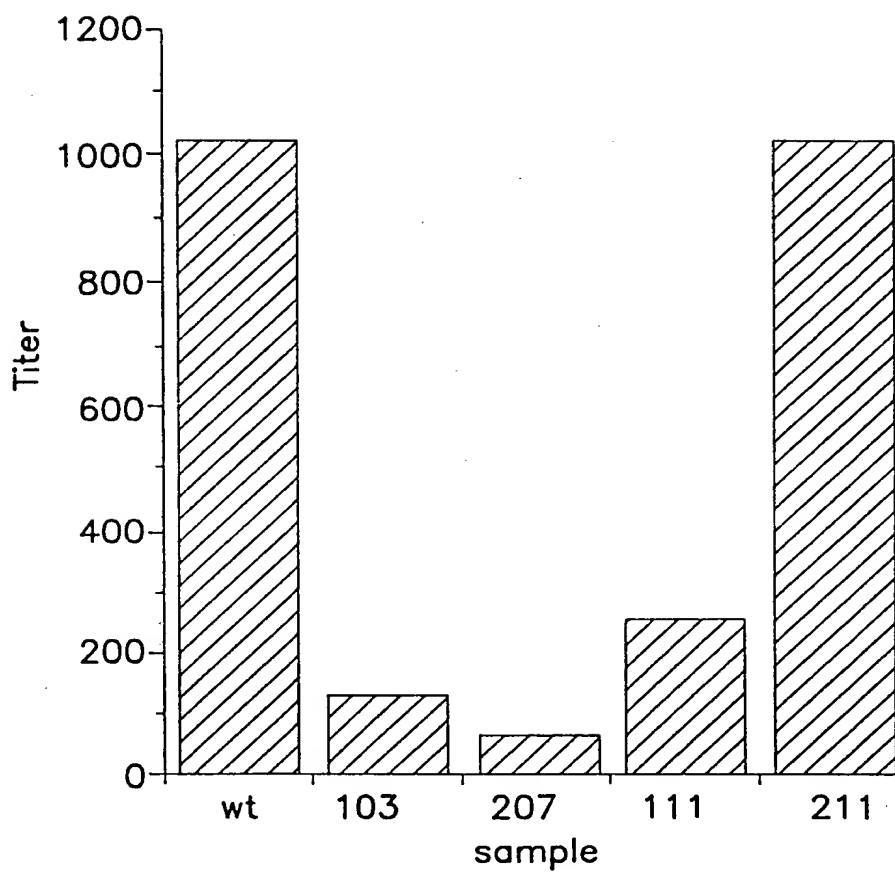


FIG. 13



18 / 23

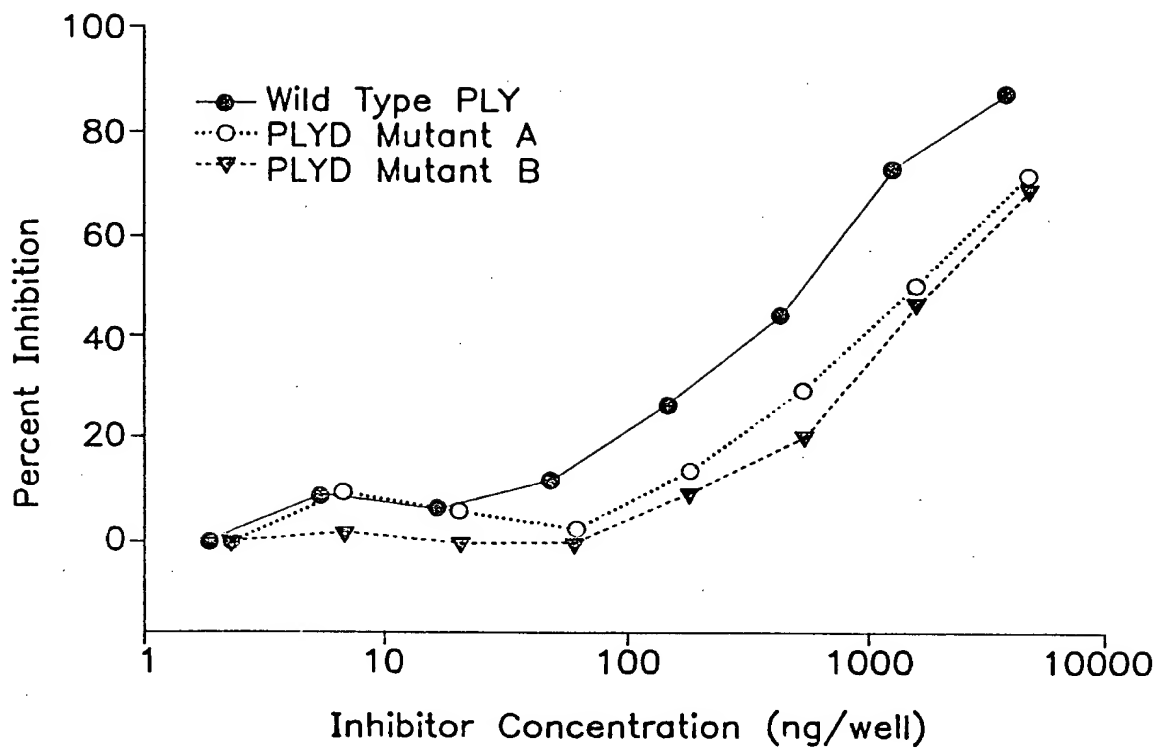


FIG. 14

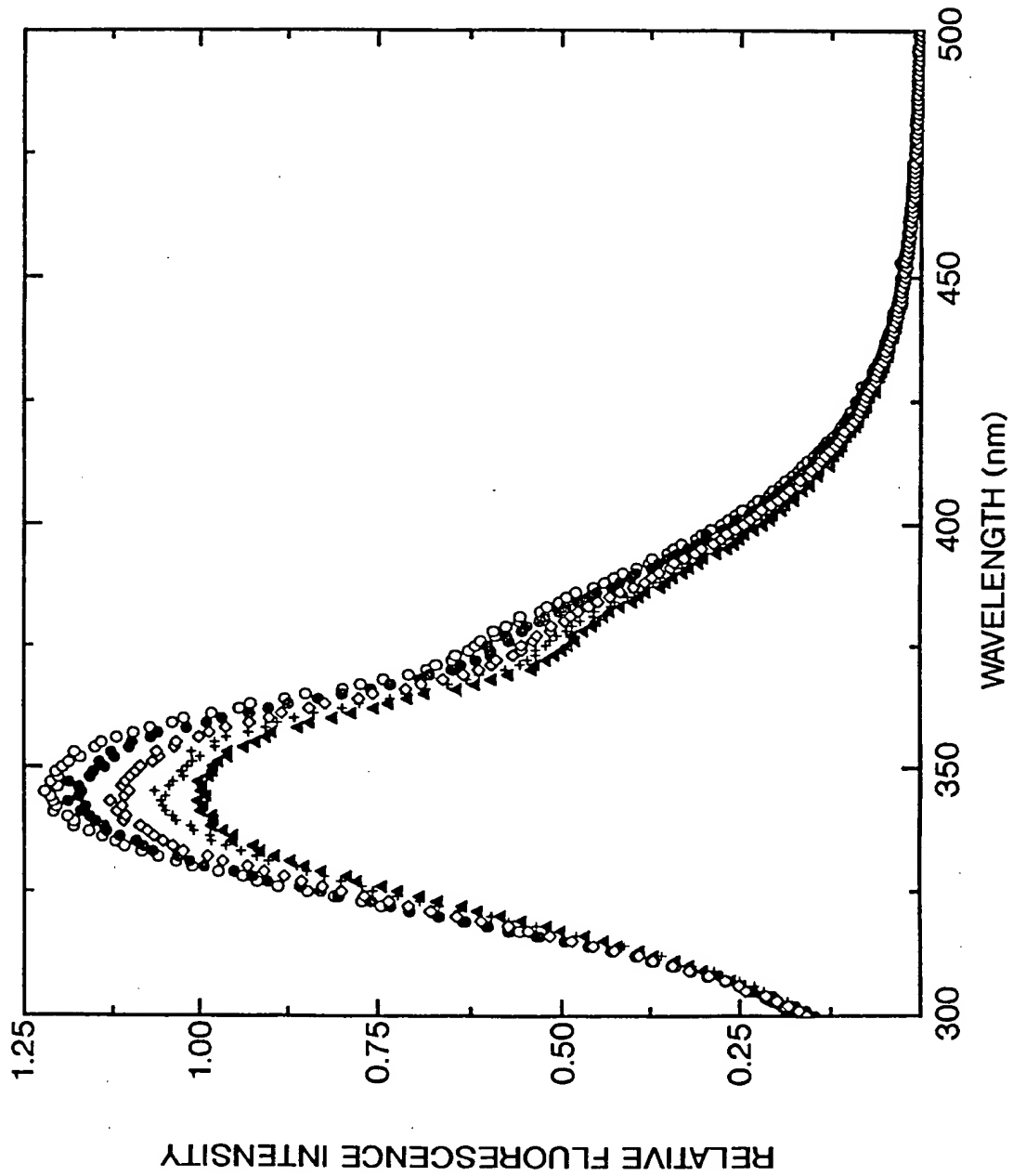


FIG. 15



20 / 23

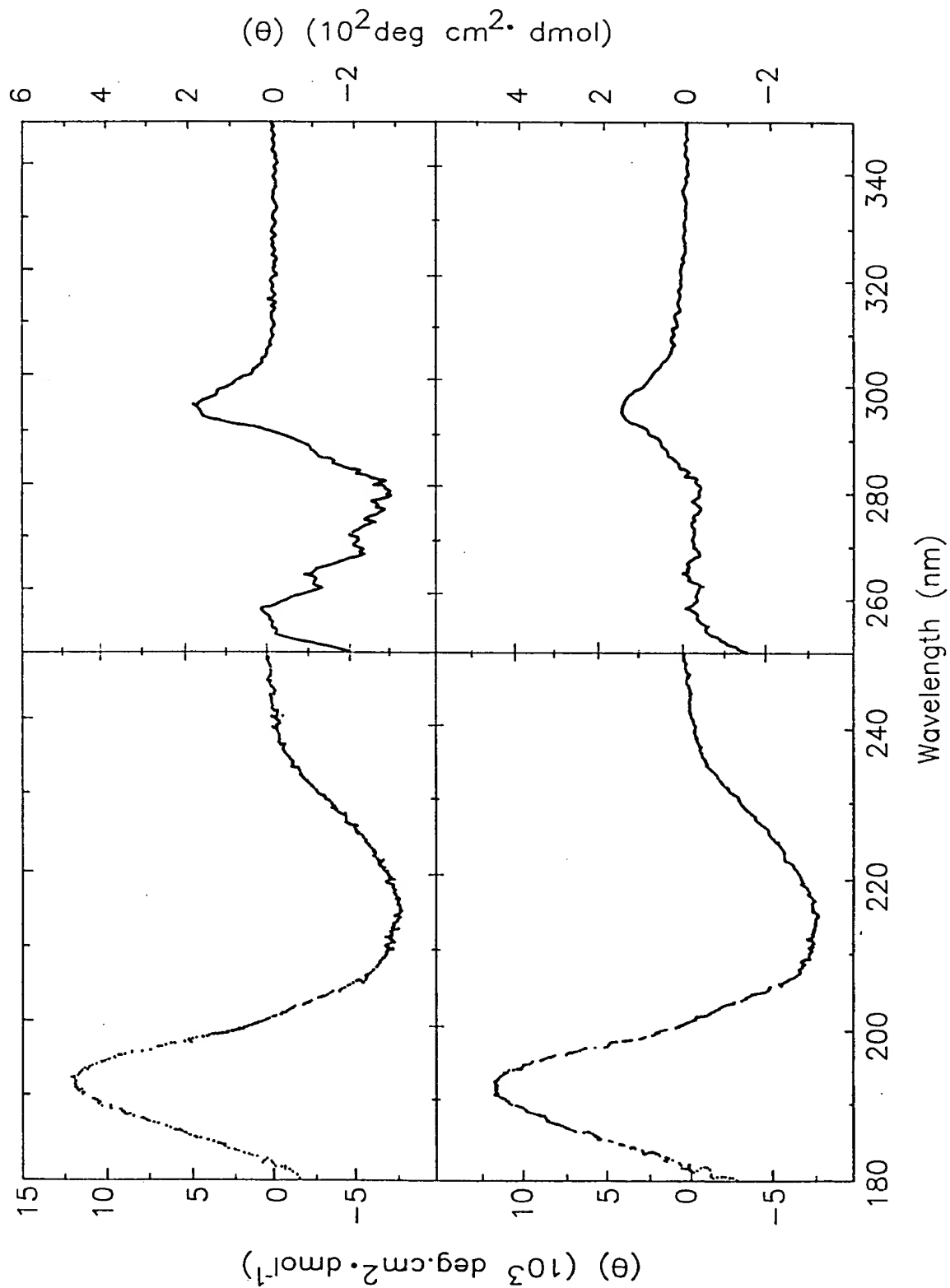
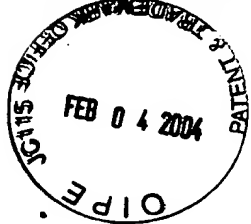


FIG. 16



21 / 23

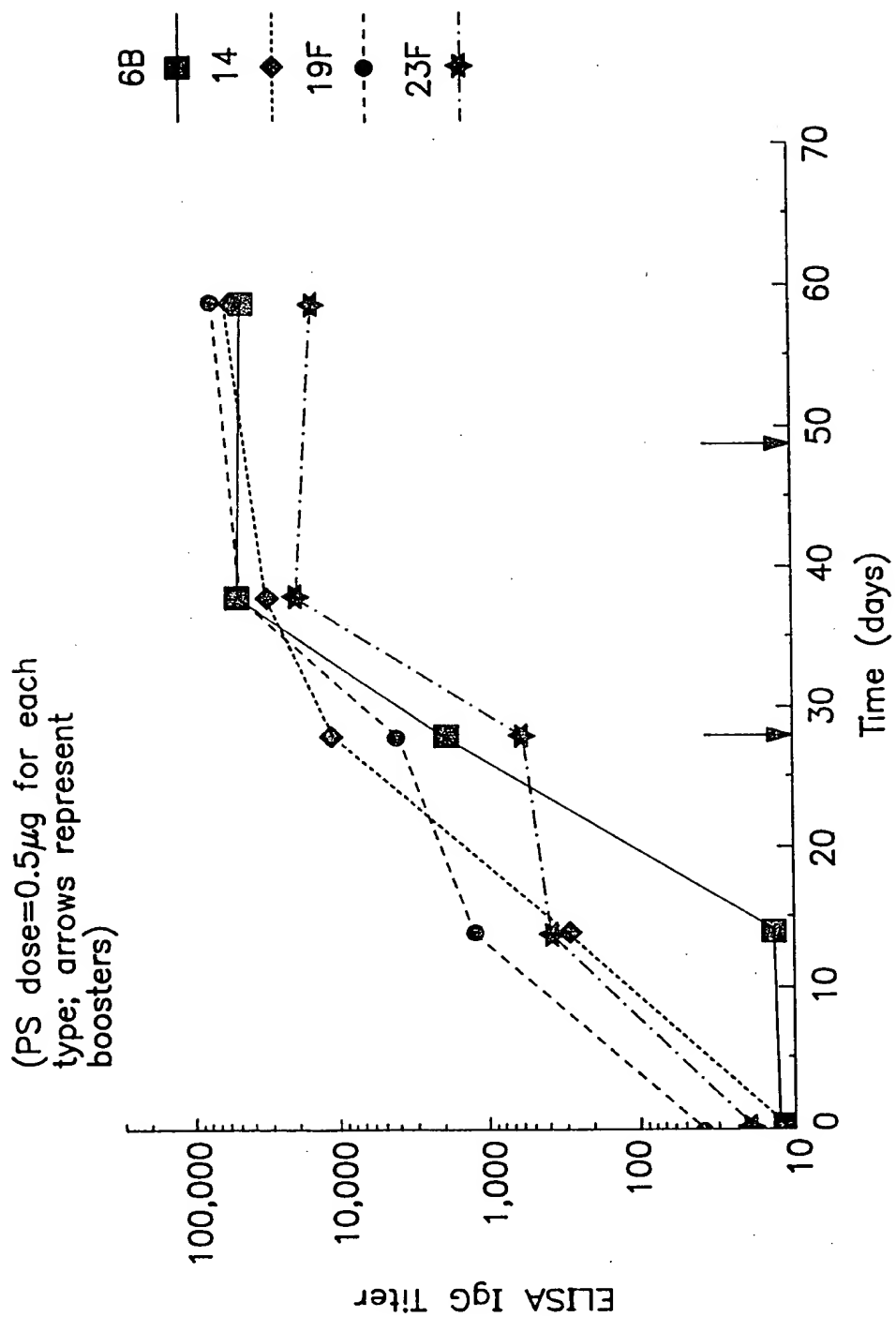
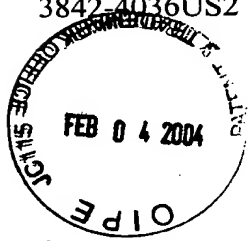


FIG. 17A



22 / 23

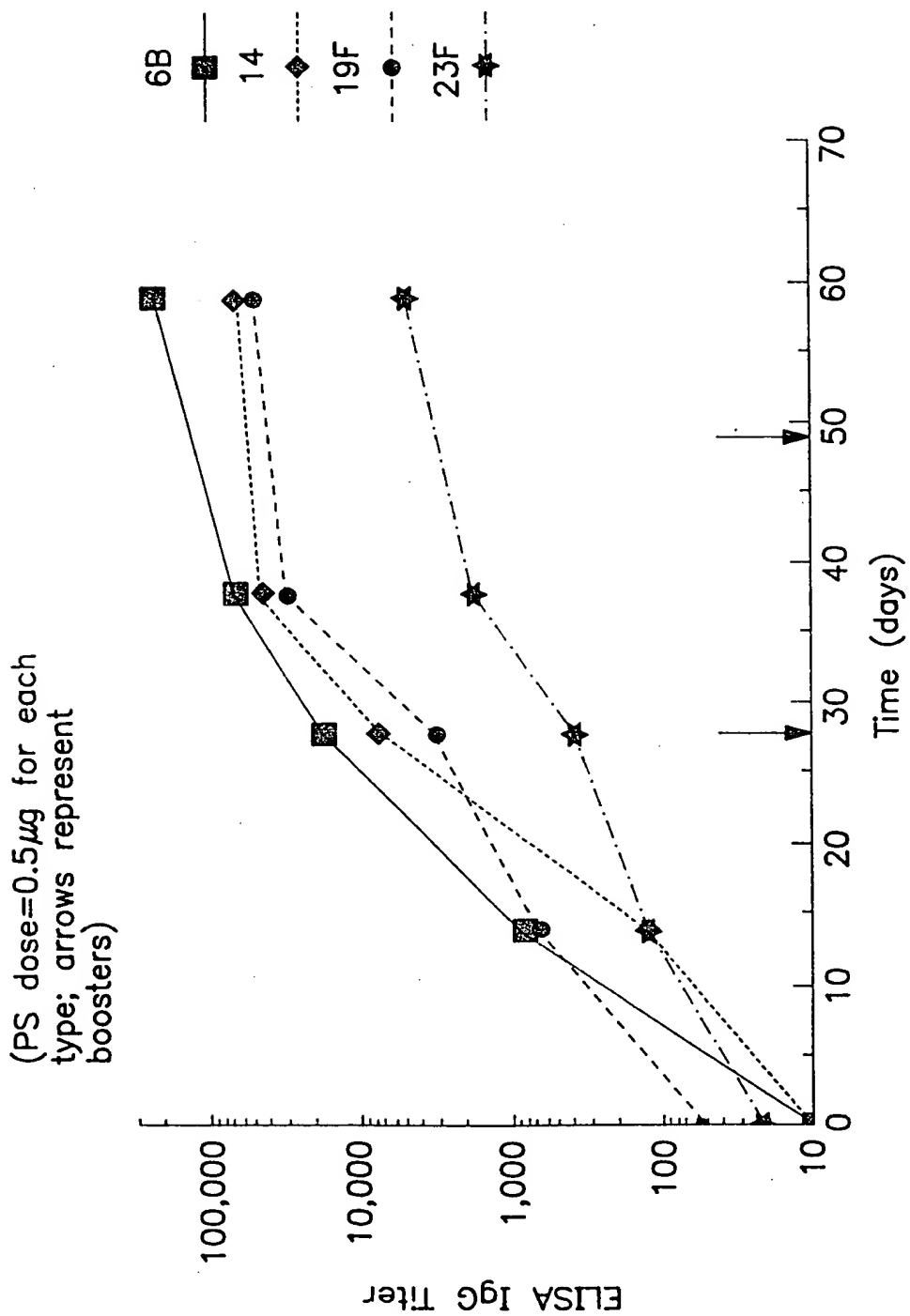


FIG. 17B

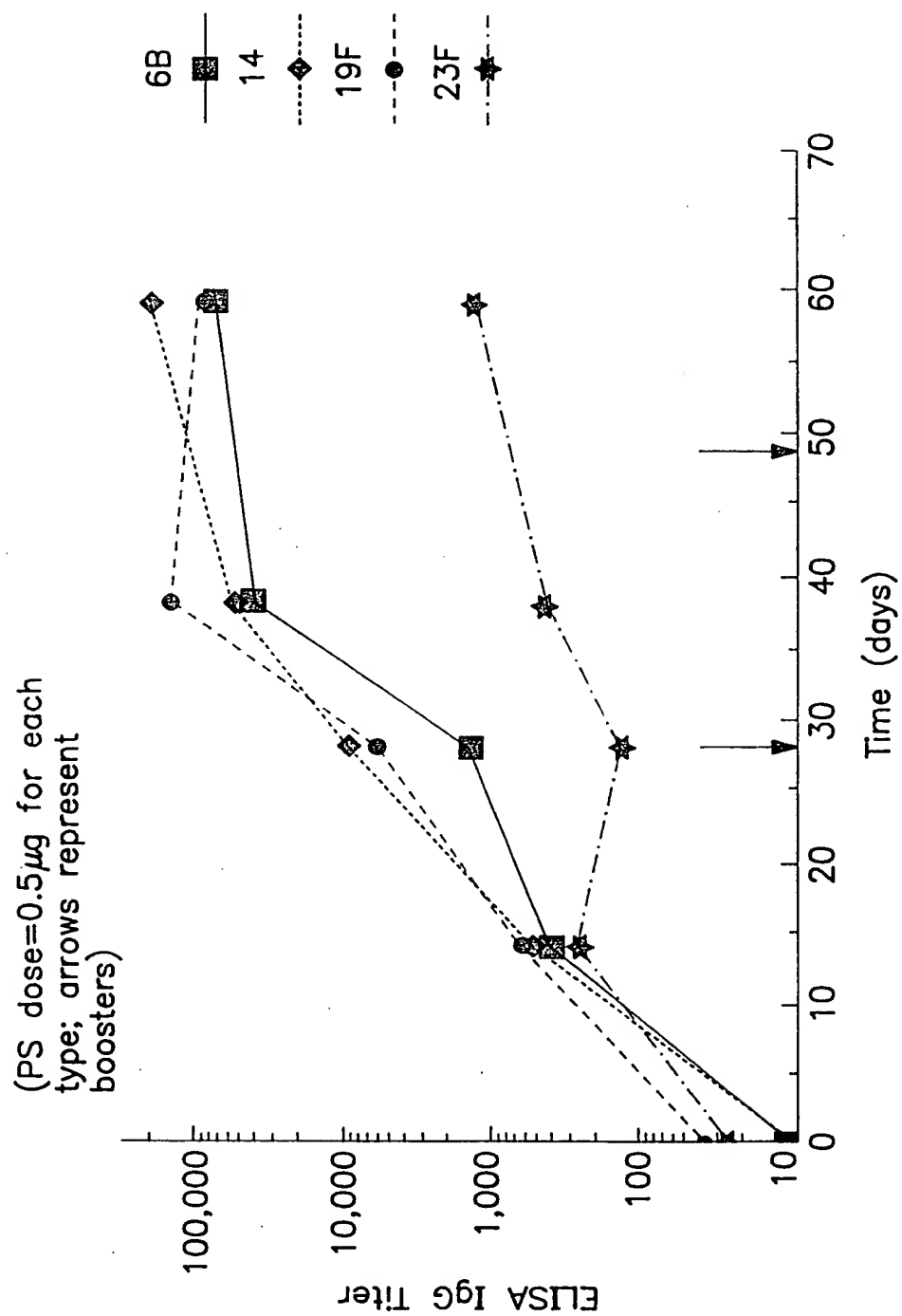


FIG. 17C

